Salvage Procedures after Restorative Proctocolectomy: A Systematic Review and Meta-Analysis

George E Theodoropoulos, MD, PhD, FACS, FASCRS, Eran N Choman, MSc, Steven D Wexner, PhD (Hon), FACS, FRCS, FRCS(Ed)

Restorative proctocolectomy with ileal pouch—anal anastomosis (IPAA) construction for ulcerative colitis (UC) or familial adenomatous polyposis can be plagued by a multitude of complications. These problems can lead to pouch failure or poor function.[1-12] The initial misdiagnosis of UC instead of Crohn's disease (CD) can also contribute to IPAA complications.[13] There are several circumstances in which a salvage procedure (SP) is necessary to resolve a complication and to prevent pouch failure. Depending on the complication, a variety of pouch-salvage techniques have been used.[7-12] However, no definitive evidence exists on which treatment strategy is the most appropriate. Surgical treatment can be tailored to suit clinical manifestations and be individualized to optimize outcomes.

The majority of relevant studies have reported on results of SPs performed on select groups of patients at single institutions. Previously published reviews have been mainly narrative, without using analytic statistical methods.[8-12] No systematic review or meta-analysis exists for the outcomes of the SPs, either overall or by category of SP.

The purpose of this systematic review was twofold: first, to systematically record the entire gamut of interventional options, both innovative and conventional, for pouch salvage after IPAA complications; and second, to provide the most current collective estimates of SP outcomes, such as their healing and function success rates.

METHODS

Data sources and search strategy

An electronic search of Medline, Scopus, and Google Scholar was performed from 1978 (first publication on IPAA) to 2013. The MeSH search headings used were "restorative proctocolectomy" and "re-operations." The following text searches, key words, and their combinations were also used: "salvage," "redo," "revision," "complications," "pouch failure," "pouch dysfunction," "pelvic sepsis" "pouch-vaginal fistula," "ileal pouch," "IPAA," and "ileal pouch-anal anastomosis." The related articles function was used to broaden the search. A cross-reference search was also conducted, after full-text articles were selected, and the reference lists of all relevant publications were also manually searched.

Study selection

For all analyses conducted in this review, studies were included only if they reported on the primary outcomes, which were the healing success rates of either SP overall or of SP categories. Studies limited to pouch excisions or re-diversions of IPAA as the only reoperative interventions, or focused on pouch failures and not on outcomes of salvage attempts, were excluded.

Due to the diversity of salvage techniques, the data were considered in the following ways: as overall SPs; as SP subtypes; and as individual SPs. Overall SPs referred to the total number of patients reported in each publication undergoing any type of procedure for pouch salvage. The SPs were classified to the following subtypes: redo SPs, which included abdominal exploration, resection of the existing pouch, and de novo creation of a pouch of any configuration accompanied by an IPAA anastomosis; revisional SPs, which included abdominal exploration and correction of the pouch pathology, including excision or oversewing of fistulas and/or pouch reduction or augmentation, with or without abdomino-anal advancement, and with or without disconnection of the old anastomosis and

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From the Department of Colorectal Surgery, Cleveland Clinic Florida, Weston, FL.

Correspondence address: Steven D Wexner, PhD (Hon), FACS, FRCS, FRCS(Ed), Department of Colorectal Surgery, Cleveland Clinic Florida, 2950 Cleveland Clinic Blvd, Weston, FL 33331. email: wexners@ccf.org

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Abbreviations and Acronyms

CD = Crohn's disease
IPAA = ileal pouch-anal anastomosis
OR = odds ratio
PVF = pouch-vaginal fistula
QoL = quality of life
SP = salvage procedure
UC = ulcerative colitis

creation of a new one; and local/perineal SPs, consisting of any procedures that did not require entrance into the abdominal cavity and were completed via the perineal, transanal, transvaginal, or transgluteal route by operative, endoscopic or imaging-guided means. Revisional and local/perineal SPs were further subclassified into individual techniques, for instance, efferent limb excision, abdomino-anal advancement, and dilation of strictures.

Analyses were performed to separately investigate the outcomes of SPs overall, of their subtypes, and of the identified individual techniques. When multiple studies were reported by the same institution, either the most complete and most recent study, or the study that comprised the largest number of patients was included in the overall data retrieval and analysis. Multi-reporting institutions' studies containing pertinent data on isolated techniques, which had not been included in the overall analysis, were maintained for the subtype or the individual technique analyses.

Only series encompassing >10 patients in the respective study cohort were included in the overall review and analysis. All relevant articles, including small case series and case reports, were included in the subtype and individual technique reviews. However, a sensitivity analysis for the primary outcomes was also undertaken, including only mutually exclusive institution series with >50 patients.

Data extraction and outcomes of interest

Relevant data, including first author, institution, year of publication, number of patients undergoing an SP, and pathologic diagnosis, were extracted according to a prespecified protocol. Indications for the SPs were classified as "septic," "mechanical," "inflammatory," "neoplastic transformation," and "not documented." Primary outcomes measures were successful healing rates of SPs overall and of subtype and individual salvage techniques. Secondary outcomes of interest were functional success rates, parameters of pouch functional outcomes (ie, daytime and nighttime number of bowel movements, leakage, nighttime soiling, urgency, use of pads, continence, use of antidiarrheal medications, and dietary restriction), SP morbidity, reoperations after SPs, and failure of SPs (eg, post-SP pouch excision, long-term or permanent diversion, incontinent pouch, and recurrence of pathology). Tertiary outcomes of interest incorporated in the span of this search were patient satisfaction rates and quality of life (QoL) outcomes.

All pertinent information was tabulated in separate data entry forms for the overall and the 3 defined SP subtypes and the index of individual techniques. The methodologic quality of studies was assessed according to the Oxford Centre for Evidence-Based Medicine guidelines for "Levels of Evidence and Grades of Recommendation," with studies assessed as addressing treatment benefits.[14]

Statistical analysis

Relevant study characteristics and outcomes were extracted for each study individually and presented by institution of origin and by reported individual techniques. First, for each variable or result, a summary statistic was calculated from each study to describe the observed intervention effect. Then a summary (pooled) intervention effect estimate was calculated as a weighted average (based on the sample size of each study) of the intervention effects estimated in the individual studies. For outcomes, pooled estimates were calculated with 95% CI. Results were summarized as mean values ± SD for continuous data and percentages (95% CI) for dichotomous data.

For individual studies that provided data for outcomes after separate SP subtypes, meta-analyses were carried out for the dichotomous outcomes variable "healing/nonhealing" using odds ratios (OR) with 95% CI as the summary statistics. The following analyses were undertaken: redo vs revisional, redo vs local/perineal, and revisional vs local/perineal. To combine the OR for the outcomes of interest, the DerSimonian and Laird method for random-effects meta-analysis was used.[15] In the random-effects model, it was assumed that each study had its own true exposure effect and that there was a random distribution of the studies' exposure effects around a central effect. Yates correction was applied for those studies that contained a zero in one cell for the number of events of interest in one of the two groups. Studies were omitted from the meta-analyses of outcomes if there were no events for both groups. In the graphical presentation of the results (Forest plots), squares indicate point estimates of treatment effect (OR), with the size of the square representing the weight attributed to each study, and 95% CI indicated by horizontal bars. The diamond represents the summary ORs from the pooled studies with 95% CI.

Three strategies were used to quantitatively assess heterogeneity. First, graphical exploration with funnel plots was performed to evaluate publication bias. Second, data were reanalyzed by using both random-effects and fixed-effects models. In contrast to the random-effects model, the fixed-effects model estimates a difference underlying a true effect and the distribution of the studies' effects follows a normal distribution. Third, Cochran's Q and I^2 were calculated.

For secondary outcomes of interest (such as function success rates, morbidity, etc), such a meta-analytic methodology performed for the successful healing rates

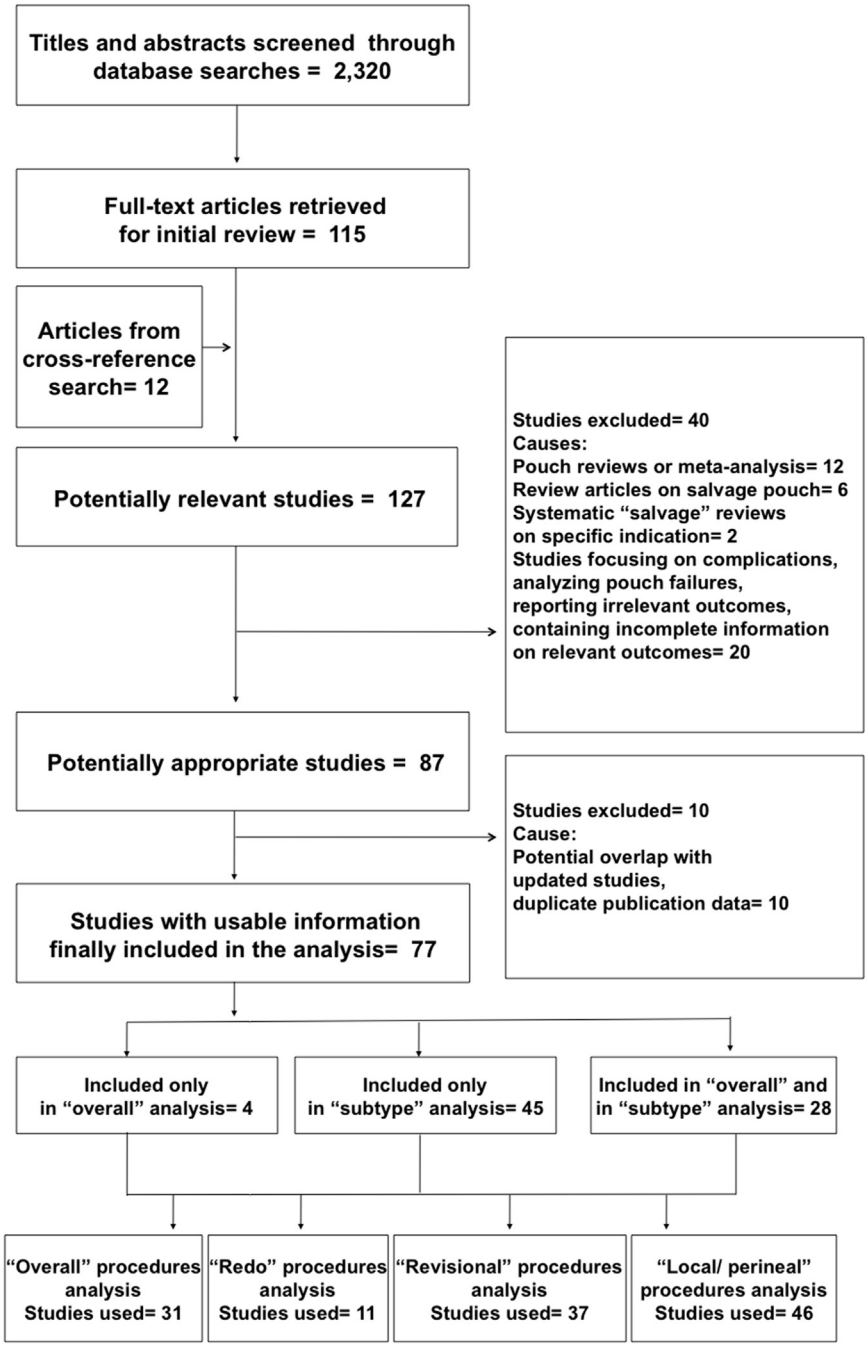


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow chart explaining the literature search strategy and studies' selection

Table 1. Study and Patient Characteristics According to the Institution of Origin

Institution	Year of publication	Inclusion period	Salvage procedures, n				Mean age, y	Sex, % female	Indication for salvage procedure			Previous salvage procedures†	Time from initial RP, mo	With defunctioning ileostomy‡
			Overall	Redo	Revisional	Local/ perineal			n*	Septic	Mechanical			
Cleveland Clinic Foundation, Ohio	2004[63] 2009[83] 2011[89] 2012[93]	1983–2009	351	71	170	110	37	51.1	329	183	135	141/351 patients Dilations: 1.74 ± 1.19 per patient (1–5)	34	66/71
St Mark's Hospital, London, UK	1996[31] 1996[32] 2005[69] 2006[73]	1976–2003	229	7	130	92	NA	63.7	216	93	123		36	24/64
Mayo Clinic, Minnesota	1990[25] 1998[43] 2009[81]	1981–2008	203	9	73	121	30.5	54.0	243	146	97	113/238 patients, 1–13 per patient	28	41/114
Mount Sinai Hospital, Toronto, Canada	2002[55] 2005[72] 2007[76]	1981–2003	138	19	50	69	32	72.7	164	0	164		18	
UCLA School of Medicine, California	1999[47]	1978–1998	164	7	157	0	NA	NA	137	118	19	10/57 patients Dilations: 39/39 patients >2 per patient (2–18)	24.8	60/141
University of Heidelberg, Germany	2002[54]	1988–1999	107	NA	NA	NA	NA	NA	90	41	49		51	NA
UK National Ileal Pouch Registry	2010[85]	1976–2006	127	NA	NA	NA	39	48.0	107	107		2.2 per patient	NA	NA
St Antoine Hospital, Paris, France	1996[33] 2005[67]	1984–2002	85	25§	20§	19§	35	77.3	85	68	17	3 per patient (1–8)	2.5	6/21
Cleveland Clinic Foundation, Florida	2009[79]	1998–2007	59	15	16	28	43	57.9	60	40	19	2.1 per patient (1–10)	NA	NA
Northwest Colon and Rectal Clinic Survey	2004[62]		52	2	22	28	NA	NA	52	0	52	NA	NA	NA
Mount Sinai Medical Center, New York	2003[58]	1980–2001	51	0	4	47	33	60.8	51	51	0	27/51 patients ≥2 per patient	NA	8/51
The General Infirmary at Leeds, UK	1994[29] 2011[90]	1983–2009	50	0	0	50	NA	100	50	11	39	NA	3	NA
Queen Elizabeth Hospital, Birmingham, UK	1993[26] 1997[36]	1983–1995	47	6	8	33	30	62.5	55	40	15	NA	NA	13/17
Lahey Clinic, Massachusetts	1998[20]	1980–1986	30	0	0	30	NA	NA	30	11	19	NA	NA	NA
Boston University, Massachusetts	1999[48]		29	9	9	11	36	58.6	29	15	14	NA	NA	NA
University of Utah	2000[50]	1983–1999	16	0	16	0	NA	50.0	18	11	5	10/16 patients	NA	4/16

(Continued)

Table 1. Continued

Institution	Year of publication	Inclusion period	Salvage procedures, n				Mean age, y	Sex, % female	Indication for salvage procedure			Previous salvage procedures†	Time from initial RP, mo	With defunctioning ileostomy‡
			Overall	Redo	Revisional	Local/perineal			n*	Septic	Mechanical			
Rush-Presbyterian St Luke's Medical Center, Chicago	2002[56]		14	0	0	14	NA	NA	14	4	10	NA	NA	NA
University Hospital of Münster, Germany	2012[92]	1997–2009	12	NA	NA	NA	NA	58.3	12	11	1	6/12 patients, 3 per patient (1–10)	NA	NA
Overall			1,764	170	65	652	35	62.6	1,742	950	778	NA	24.6 ± 16.6	222/495

Only studies including >10 patients are represented.
*Total number of patients with reported indication for salvage procedure.
†Number of patients with multiple salvage attempts, mean number (range) of salvage procedures/patient.
‡When salvage procedure required or complication occurred (number of patients/number of patients evaluated).
§Among the patients included in Dehni and colleagues,[67] 33 procedures for 11 patients reported in Lolohea and colleagues[11] were not included due to inability to calculate number of patients/procedure subtype.
NA, data not available; RP, restorative proctocolectomy.

between different SP subtypes could not be applied because studies simultaneously reporting on different subtypes' secondary outcomes results were nonexistent. Therefore, results for those outcomes variables were restricted to those derived from the initial pooled analysis. Data analysis was performed using IBM SPSS Statistics, version 20 and the Comprehensive Meta-Analysis, version 2 (Biostat) software.

RESULTS

Selection process

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart explaining the literature search strategy and study selection[16] are shown in Figure 1. Selections based on exclusion criteria resulted in a total of 77 studies, including 2,103 patients who underwent SPs, as eligible for inclusion in the various analyses of the current review.[17-93] This was agreed on by two authors (GT, SW).

Description of studies

Except for one matched-case study[89] and two national surveys,[62,85] the remainder of the studies were observational, reporting either retrospectively or prospectively collected data (level 4). The majority of the studies were case series (46 series), including cohorts of <10 SP patients, and 12 of them were case reports. A summary of patient characteristics and SP results is provided in Tables 1 to 5. A total of 31 studies originating from 16 institutions and 2 national surveys, presenting outcomes on 1,764 SP patients of a total of 1,987 complicated IPAA patients, were included in the overall analysis (Table 1). Complicated pouches were conservatively managed in 123 of the 521 patients from 6 institutions.[20,25,26,31,32,36,43,54,55,63,69,72,73,76,81,83,93] The distribution of the initial pouch design was J in 1,064, S in 134, W in 64, and other type in 254 patients. Ulcerative colitis was the primary diagnosis in 83.5% of the overall study population and the final diagnosis in 74%. The percentage of postoperative newly diagnosed CD among the initially diagnosed UC and indeterminate colitis patients was 11.9%. Among the 1,076 patients with available data, the primary diagnosis and respective number of patients were as follows: UC in 899 patients; CD in 9 patients; indeterminate colitis in 32 patients; familial adenomatous polyposis in 121 patients, and "other" in 15 patients. The final diagnosis was UC in 118 patients; CD in 25 patients; indeterminate colitis in 32 patients; familial adenomatous polyposis in 121 patients, and "other" in 15 patients.

The overall analysis included studies with >10 patients, with a median sample size of 48 patients (range 12 to 235

patients) during a median inclusion period of 14 years (range 2 to 25 years).

One hundred and seventy (11.3%), 685 (45.4%), and 652 (43.3%) redo, revisional, and local/perineal procedures, respectively, were performed, among the 1,507 patients for whom relevant information on the SP subtype was available (Table 1). Nine hundred and fifty (54.5%), 778 (44.6%), 8 (0.4%), and 6 (0.3%) required an SP for a "septic," "mechanical," "inflammatory" and "neoplastic" indication, respectively, among the 1,742 patients for whom the indication for SP had been reported (Table 1).

Data for the subtype analysis were derived from all studies in which the outcomes of individual SP subtypes were reported. Overall analysis was focused on studies with >10 patients. Therefore, the number of patients for the subtype analysis was different from the ones included in the overall analysis. Subtype analysis was focused on 90 cases from a total of 11 studies reporting on redo SPs outcomes,[27,32,36,46-48,60,62,67,72,79] on 531 patients reported from the 37 studies with relevant outcomes data on revisional SPs,[21,24,27,31-34,36,40-45,47-52,58,59,61,62,64,68-73,76,79,81,84,86,87] and on 676 patients from the 45 series, including local/perineal results.[17-20,26,28-30,33,35-39,43,47,48,53,54,56-60,62,63,65,66,69,72,74,75-80,82,87-93]

Outcomes

Healing success, morbidity, and failures

Salvage procedures were performed 24.6 ± 16.6 months after the initial restorative proctocolectomy. Median follow-up was 26 months (interquartile range 12 to 51.5 months). Overall and subtype analysis found pooled incidences of successful healing in 73.5% (95% CI, 67.5−79.5%), 82.2% (95% CI, 72.5−91.9%), 79.6% (95% CI, 75.7−83.5%), and 68.4% (95% CI, 57.5−79.3%) of the overall (Table 2), redo, revisional, and local/perineal procedures, respectively. Eleven studies provided outcomes data on separate SP subtypes (Fig. 2). Meta-analysis of healing rates did not demonstrate significant differences in healing rates between revisional SPs vs redo SPs, redo SPs vs local/perineal SPs and revisional SPs vs local/perineal SPs (Figs. 2 and 3).

Morbidity was 41.4% (95% CI, 21.7−61.2%) for the overall procedures (Table 2) among the 960 SP patients reported in 12 studies from 9 institutions.[25,32,43,47,50,55,67,72,73,81,83,89] Among a total of 347 reported complications, the most common were pouch fistula (15.2%), stricture (13.5%), pelvic abscess (10%), pouchitis (9.2%), wound infection (9.2%), small bowel obstruction (8.3 %), and pouch-vaginal fistula (6.9%). Revisional SP, as reported in 10 studies that included 258 SP patients, resulted in higher complication rates than did local/perineal procedures (44.2%; 95% CI, 13.6−74.7% vs 13.6%; 95% CI, 0−66.1%). Calculation for the redo procedures was not performed, as there was only one relevant study. Failure rates of SP were higher for local/perineal (21.3%; 95% CI, 11.7−31%) compared with revisional SP (15.7%; 95% CI, 10.9−20.4%). Among a total of 927 SP patients included in the 17 studies reporting on failure rates, 18% eventually underwent pouch excision (110 patients) or permanent diversion (57 patients). A number of reoperations after SP were also performed, which, except for pouch excisions and rediversions, at least in the studies reporting them in detail, mainly consisted of repeat local/perineal approaches. After excluding the 2 surveys, when only the 11 most representative from each multi-reporting institution studies including >50 patients were analyzed, the healing success rate was 76.3% (95% CI, 69.2−83.5%).

Functional outcomes

Functional success was achieved in 71.9% (95% CI, 60−83.8%), 83.9% (95% CI, 55.6−100%), 75.8% (95% CI, 69.1−82.5%), and 71% (95% CI, 40.6−100%) of patients included in the overall, redo, revisional, and local/perineal studies' analysis, respectively (Table 2). Twenty-one of the 77 studies in this review disclosed information on one or more functional parameters or variables (Table 3).[21,25,32,33,36,43,47,50,55,64,67,73,81,83,85,89,92] Outcomes of individual revisional and local/perineal SPs are summarized in Table 4.

A proposed algorithmic approach accompanied by relative success rates of the various salvage options is presented in Figure 4.

Quality of life outcomes and patient satisfaction

Information on QoL outcomes related to the performance of SP was retrieved from 11 studies from 9 institutions (Table 5).[36,43,48,55,63,67,68,83,84] Specifically designed or validated questionnaires were formally used in most of the studies. Patient satisfaction rates were given in 6 studies from 4 institutions (Table 5).

DISCUSSION

The number of SPs attests to both the variety of their indications and to the lack of full efficacy of any one of the operations. Pouch complications themselves consist of heterogeneous entities and vary in clinical severity. This fact likely accounts for the lack of comparative and controlled studies focusing on SP after IPAA. The overwhelming body of evidence in this field consists of retrospective cohort series. This finding is in keeping with previously published meta-analyses on primary IPAA results.[3,4] Despite the overinterpretation related to the inherent

Table 2. Results Obtained with the Application of Salvage Pouch Procedures According to the Institutions of Origin of Each Study

		Healing rates		Morbidity		Reoperations		Failures		Functional success rates	
Institution	Follow-up period, mo	Evaluated, n	Pooled incidences, %	Evaluated, n	Pooled incidences, %	Evaluated, n	Pooled incidences, %	Evaluated, n	Pooled incidences, %	Evaluated, n	Pooled incidences, %
Cleveland Clinic Foundation, Ohio	46.5	351	81.1	235	33.2	255	35.8	235	16.9	85	82.4
St Mark's Hospital, London, UK	40.0	229	58	112	19.5	160	21.3	160	17.5	128	81.3
Mayo Clinic, Minnesota	48.5	203	73.4	64	65	178	30	178	25.6	165	58.8
UCLA School of Medicine, California	7.7	164	78	164	56.1	NA	NA	NA	NA	164	88.4
Mount Sinai Hospital, Toronto, Canada	64.6	138	66.7	79	49.4	138	21	79	26.6	79	67.1
UK National Ileal Pouch Registry	58.0	127	69.3	NA	NA	NA	NA	NA	NA	NA	NA
University of Heidelberg, Germany	NA	107	83.2	NA	NA	NA	NA	NA	NA	NA	NA
St Antoine Hospital, Paris, France	33.0	85	77.6	58	10.9	79	11.8	79	25.9	79	58.8
Cleveland Clinic Foundation, Florida	18.0	59	62.7	NA	NA	59	13.6	59	15.3	NA	NA
Northwest Colon and Rectal Clinic Survey	NA	52	98.1	NA	NA	NA	NA	52	1.9	52	94.2
Mount Sinai Medical Center, New York	42.0	51	41.2	NA	NA	NA	NA	NA	NA	NA	NA
The General Infirmary at Leeds, UK	25.0	50	76	NA	NA	11	72.7	11	14	NA	NA
Queen Elizabeth Hospital, Birmingham, UK	34.5	47	70.2	NA	NA	30	10	30	30	16	53.3
Lahey Clinic, Massachusetts	NA	30	83.3	NA	NA	30	20	30	13.3	NA	NA
Boston University, Massachusetts	30.0	29	58.6	NA	NA	NA	NA	NA	NA	29	58.6
University of Utah	24.0	16	100	16	50	16	12.5	NA	NA	16	87.5
Rush-Presbyterian St Luke's Medical Center, Chicago	NA	14	92.9	NA	NA	NA	NA	14	7.1	NA	NA
University Hospital of Münster, Germany	NA	12	66.7	NA	NA	NA	NA	NA	NA	12	66.7
Overall, n		1,764		728		956		927		825	
Overall pooled estimates	39.2 ± 20.74*		73.5 (67.5–79.5)†		41.4 (21.7–61.2)†		27.1 (12.5–41.7)†		19 (14.6–23.4)†		71.9 (60–83.8)†

Only studies including >10 patients are represented. A total of 31 studies, originating from 16 institutions and 2 national surveys, presenting outcomes on 1,764 salvage procedure patients are demonstrated. Respective references for each included institution are reported in Table 1.

*Values are mean ± SD.

†Values are % (95% CI).

NA, data not available.

Table 3. Functional Outcomes of Salvage Procedures Overall According to Institution of Origin

	Daytime BMs		Nighttime BMs		Leakage		Nighttime soiling	
Institution	Evaluated, n	Weighted mean	Evaluated, n	Weighted mean	Evaluated, n	Pooled incidences, %	Evaluated, n	Pooled incidences, %
Cleveland Clinic Foundation, Ohio	148	7.3	95	3.9	148	44.1	95	60
St Mark's Hospital, London, UK	48	6	32	0.7	16	6.3	16	12.5
Mayo Clinic, Minnesota	263	5	89	1	114	13.2	114	28.1
UCLA School of Medicine, California	164	4	NA	NA	164	7.9	NA	NA
Women's College Hospital, Toronto, Canada	57	8	NA	NA	NA	NA	57	66.7
UK National Ileal Pouch Registry	39	6	NA	1	39	2.6	39	7.7
St Antoine Hospital, Paris, France	79	6	21	1	79	17.7	79	38
The General Infirmary at Leeds, UK	39	5	NA	NA	39	38.5	NA	NA
Queen Elizabeth Hospital, Birmingham, UK	47	10	NA	NA	47	14.9	47	14.9
University of Utah	16	7	NA	NA	NA	NA	16	56.3
Overall, n	912		237		646		463	
Overall pooled estimates		6.5 ± 1.48*		1.8 ± 1.82*		21.9 (8.9–35)†		38.4 (21.7–55.2)†

and unavoidable heterogeneity of the studies, the pooled estimates of outcomes measures in our review can represent the approximate results of various SPs. That can assist the clinician to comprehend what to expect after an SP is performed, based on the current available knowledge.

Types of salvage procedures

In conjunction with appropriate patient selection, surgical judgment, and individual surgeon experience, the decision as to which technical approach to use is problem specific and is largely influenced by the indication for SP.[55,79] Failure of one salvage attempt should not be considered a contraindication to additional attempts; this admonition is supported by the number of patients who underwent SPs.[19,29,50,51,54,55,58,63,67,70,76,77,79,83,92]

Taking into consideration the heterogeneity of SPs, we subdivided overall salvage into subtype and individual analyses. Several studies reported on cohorts with several types of SPs, without reporting on separate subtype outcomes, which precluded the inclusion of multiple studies in the meta-analysis performed between different subtypes. This also prohibited inclusion of these studies into the subtype pooled analysis. No statistical significance among different SP subtypes was found in the meta-analysis of the rather limited number of studies separately reporting on different subtypes healing rates.

Procedure-related variables, such as the magnitude of the intervention, the extent of the anatomic dissection, the magnitude of the physiologic stress, and the requirement for loss of diseased small bowel, can categorize SPs into the cohesive groups of redo, revisional, and local/perineal SPs. Favorable results in terms of healing rates were demonstrated in descending order for the redo, revisional, and local/perineal SP included in the overall analysis, with mean percentages of 82.2%, 79.6%, and 68.4%, respectively. Several considerations should be taken into account when critically evaluating these results. Patients selected for a local SP might have a less severe pathology, which can inadvertently lead to a bias in favor of the local/perineal approaches. Local approaches might not be adequate for the correction of the responsible pathology. However, due to the considerably lower morbidity rate associated with the performance of a local/perineal SP, as demonstrated in our review (13.6% vs 44.2% for the revisional SPs), some authors have suggested that all revisional surgery should be first attempted transanally, with the aim of local repair.[44] Although a transanal approach might suffice, the rate of reoperations to achieve the desirable outcomes, according to our results, is almost 3 times higher than after revisional abdominal surgery.

In important informative studies from a number of institutions, redo and revisional SP results are collectively reported as abdominal approaches, with highly satisfactory success rates for septic or for nonseptic complications (74% to 85%).[55,73,83] The revisional abdominoperineal approach has been proposed as the most preferable first option when dealing with pouch septic complications, especially with pouch-vaginal fistula (PVF).[55] This preference is based on the high success rate of the abdominal approach,

Table 3. Continued

Continence rates		Urgency		Use of pads		Use of antidiarrheal medications		Dietary restriction	
Evaluated, n	Pooled incidences, %	Evaluated, n	Pooled incidences, %	Evaluated, n	Pooled incidences, %	Evaluated, n	Pooled incidences, %	Evaluated, n	Pooled incidences, %
151	79.2	148	44.5	148	41.2	NA	NA	95	29.7
48	89.1	32	6.3	32	18.6	32	46.9	NA	NA
203	66	NA	NA	38	42.1	38	71.1	NA	NA
NA	NA	164	15.2	NA	NA	NA	NA	NA	NA
57	92.2	57	17.5	NA	NA	NA	NA	NA	NA
NA	NA	39	5.1	39	10.3	39	48.7	NA	NA
58	82.4	58	27.6	21	28.6	58	75.9	58	69
NA	NA	NA	NA	39	35.9	39	48.7	NA	NA
47	44.7	NA	NA	30	20	NA	NA	NA	NA
NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
564		498		347		206		153	
	76.5 (61–92.1)†		26 (7.4–44.6)†		32.6 (17.4–47.7)†		58.3 (36.2–80.3)†		40.8 (0–92)†

Only studies with >10 patients are represented. A total of 31 studies originating from 16 institutions and 2 national surveys are presented.
*Values are mean ± SD.
†Values are % (95% CI).
BM, bowel movement; NA, data not available.

the technical difficulties of endoanal flap advancements in patients with stapled IPAA, and the avoidance of potential sphincter trauma from repeated local procedures.[55]

Pelvic sepsis, Crohn's disease

Sepsis was found to be the principal indication for SP in our analysis. Three of the included studies in our review have specifically addressed the worse outcomes after SP for a septic compared with a mechanical indication.[25,36,73] Repair of pouch defects, removal of fibrotic and necrotic pelvic tissues, and abdominoanal advancement of the preserved pouch, are the integral components of revisional SP for a septic indication.[9,44,55,73,79,81] Such a strategy results in success rates of 66.7% to 86%.[44,61,72] Every effort should be made to preserve the "old" pouch and as much bowel as possible; otherwise a redo surgery should be used.[55,67,73]

In our review, the percentage of newly diagnosed CD patients was 11.9% among those who had been initially operated on for UC. The differentiation between CD and IPPA-related complications might also be difficult to discern.[94-96] Although patients with CD can have favorable long-term outcomes after redo IPAA, CD of the pouch is associated with risk of primary restorative proctocolectomy/IPAA failure rates from 16% to 45%.[97-100] Indirect evidence for the association between CD and unsuccessful surgery is derived from the reported experience of 4 of the institutions included in our review.[73,79,81,83]

Pouch-vaginal fistula

Two meta-analyses focusing on post-IPAA PVFs have been published.[11,12] Three of the reports[101-103] included in the latest Maslekar and colleagues[12] meta-analysis were not included in our study because their results might have been duplicated by updated publications from the same institutions.[60,69] We included 3 other studies[17,76,79] on PVFs in our review, which had not been incorporated in the Maleskar and colleagues analysis. In agreement with this published meta-analysis, the transabdominal procedures appear to be associated with a greater chance of success (72%) and, when compared with other options, with the least probability of reintervention (15%).[12,26,60,69,46,55,72]

Several studies provided clear outcomes of ileoanal advancement for PVFs,[26,28,41,60,74,76] approximately half of the patients will benefit from this procedure. Scrutinizing the individual techniques reported in our review, we found a success rate of only 33.3% for the transvaginal repair,[60,69,72] in contrast to the reported success rate of 57%[12]; this contradiction should be attributed to the inclusion of Burke and colleagues' favorable initial results that were not reproducible in later reports from the same institution.[69] Similarly, the mere advancement of an endoanal flap might not be successful under these circumstances.[72]

There is not much controversy about the fact that repairs like plain fistulectomy do not offer definitive cure and are not currently advocated, and seton placement is

Table 4. Identified Revisional and Local/Perineal Salvage Procedures

Salvage procedures	Total, n*	Indications, n	Outcomes	
			Healing rates, % of SPs (95% CI)	Functional success rates, % of SPs (95% CI)
Revisional				
Pouch repair with/without pouch disconnection and abdomino-anal advancement[31,33,34,44,50,52,58,59,61,67,69,72,73,81]	227	Pelvic sepsis/abscess, 21; anastomotic leak/separation, 10; PVF, 57; PF/sinus, 33; stenosis/stricture, 16; long efferent limb, 6; afferent limb obstruction, 25; retained rectum, 3; pouch septum, 3; twisted pouch, 5; Straight, 5; inflammatory, 2; neoplastic changes, 2	79.3 (74.6–84)	82.4 (73.2–91.6)
Partial pouch resection[27,31,32,47]	104	Pelvic sepsis/abscess, 1; PVF, 1; PF/Sinus, 1; stenosis/stricture, 88; poor emptying, 1; long efferent limb, 11; ischemic pouch, 1	76.9 (72.3–81.6)	75 (66.6–83.4)
Pouch enlargement[36,73]	75	Stenosis/stricture, 1; SVR, 13	77.9 (60.4–95.4)	93.8
Transabdominal repair of pouch prolapse, pouchopexy[36,62,70,86,87]	42	Pouch prolapse, 42	92.9 (67.8–100)	100
Efferent limb excision[21,24,31,34,36]	22	Stenosis/stricture, 1; poor emptying, 12; long efferent limb, 9	77.3 (37.1–100)	56.3 (19.8–92.7)
Conversion of straight ileo-anal to pouch anastomosis[47]	16	Sphincter dysfunction/incontinence, 16	100	100
Transabdominal drainage of pelvic abscess[43]	16	Pelvic sepsis/abscess, 16	75	
Transabdominal pouch stenosoplasty[36,41,64]	7	Stenosis/stricture, 2; long efferent limb, 5	100	100
J- to W- pouch conversion[45]	5	Sphincter dysfunction/incontinence, 5	100	100
Bypass of afferent limb obstruction[40]	5	Afferent limb obstruction, 5	60	40
Transposition rectus abdominis[49]	4	PVF, 4	100	
Gastric pouch interposition[85]	3	Ischemic pouch, 4	100	100
Jejunal interposition[42,68]	3		100	100
Inversion pouch technique[51]	2	PVF, 2	100	100
Local/perineal				
Ileoanal advancement[26,28,38,53,60,69,74,76]	91	PVF, 86; PF/Sinus, 8	58.4 (41.5–75.4)	66.7 (10.2–100)
Tranvaginal repair of PVF[60,69,72]	39	PVF, 39	33.3 (22.3–44.4)	
Fistulotomy[22,26,38,79]	24	PF/sinus, 24	92.6 (0–100)	
Seton placement[26,60,69,74]	20	PVF, 12; PF/Sinus, 8	30 (0–91.1)	
Sinus tract unroofing[37,80,93]	20	PF/Sinus, 20	70 (0–100)	
Layered suture-closure of fistula[20,38,72,93]	15	PF/Sinus, 11	33.3 (0–63.9)	
Fistula excision[26,36]	10	PF/Sinus, 10	92.6 (0–100)	
Gracilis muscle interposition[19,33,36,72,79]	14	PVF, 10; sphincter dysfunction/incontinence, 4	71.4 (31.9–100)	66.7 (0–63.1)
Fistula button plug[90]	11	PVF, 11	87.5 (0–100)	
Fibrin glue for fistula[65,72,74]	6	PVF, 3; PF/Sinus, 3	66.7 (0–100)	
Transanal flap repair[72]	5	PVF, 5	20	
Sphincteroplasty for PVF[23]	3	PVF, 3	66.7	
Permacol collagen implant[77]	1	PVF, 1	100	100
Resuturing of anastomosis[20]	6	Anastomotic leak/separation, 6		
Transanal drainage of abscess[22,33,43,56,76,79,89]	79	Pelvic sepsis/abscess, 79	73.6 (56.5–90.7)	
CT-guided drainage of abscess[43,76,89]	51	Pelvic sepsis/abscess, 51	90.2 (74.5–100)	
Endoscopic needle knife treatment[88,91]	4	Pelvic sepsis/abscess, 4	100	100
Endosponge treatment[75]	2	Pelvic sepsis/abscess, 2	100	

(Continued)

Table 4. Continued

Salvage procedures	Total, n*	Indications, n	Outcomes	
			Healing rates, % of SPs (95% CI)	Functional success rates, % of SPs (95% CI)
Dilation of strictures[18,20,29,30,35,56,59,79]	132	Stenosis/stricture, 132	65.2 (16.4–100)	75
Endoscopic balloon dilation[63]	19	Stenosis/stricture, 18	100	
Postanal repair for incontinence[36]	2	Sphincter dysfunction/incontinence, 2	0	0
Transanal division of septum[18,20,57,78,82]	16	Pouch septum, 16	100	100
Transanal resection of efferent limb[39,47]	59	Long efferent limb, 59	98.3 (97.6–99)	98.3
Transanal myotomy[17]	2	Long efferent limb, 2	100	100
Sphincteroplasty for incontinence[30]	2	Sphincter dysfunction/incontinence, 2	100	
Transanal repair of prolapse[62,66,87]	31	Pouch prolapse, 31	100	100
Not specified[76]	22			

*Number of patients with reported indications for the individual salvage procedures.
PF/Sinus, peri-pouch fistula/sinus other than PV fistula; PVF, pouch-vaginal fistula; SP, salvage procedure; SVR, small-volume reservoir; SP, salvage procedure; Straight, straight ileo-anal anastomosis.

used for control of sepsis only.[12,26,23,60] Flap procedures with gracilis muscle interposition have been reported with promise and, at least for the relatively small number of PVF patients identified among our individual techniques, its use is associated with a 75% success rate,[19,72,79] which is higher than that reported by the PVF meta-analysis.[12] The initial promising results shown by button anal fistula plug for the treatment of PVFs were not maintained at long-term follow-up.[90,104]

Mechanical indications

In our review, pouch stenosis was the predominant mechanical indication for SP. Dilations are associated with highly satisfactory success rates.[18,20,29,30,35,56,59,79] Prolapse is a less well-characterized, late IPAA complication that has been under-reported by individual institutions.[36,62,66,70,86,87] The inclusion of an important survey of the North American experience has resulted in the higher relative frequency of this condition, but has also provided useful evidence on the types and numbers of procedures used.[62]

Complications after salvage procedures

Although the complication rates of the individual series from specialized institutions vary widely,[41,47,50,55,67,72,73,83] the pooled frequency of complications after SP in the current review of about 40% is in proximity to the complication rates reported by large series and by meta-analyses for primary IPAA.[2-4] As expected, revisional surgery was related to a higher frequency of complications compared with the local/perineal procedures. One group has reported that complications were more frequent in those who had pouch excision with creation of a new pouch compared with those whose old pouch was used.[55] The rate of post-SP complications was higher in patients who had septic complications compared with those who had an outlet problem.[55]

Functional results and quality of life

Functional results are an important outcomes measure of the success of SPs. Although the bowel function variables estimated in previous primary IPAA meta-analyses were not exactly the same as the ones used in our SP analysis, SP functional results were inferior.[3,4] For example, our pooled rates of 26% and 38.4% for urgency and nighttime soiling, respectively, are worse than the reported rates of 7.3%, 17.3%, and 7.6% for urgency, mild, and severe nighttime incontinence, respectively, after initial restorative proctocolectomy.[3,4] This functional deterioration might be attributable to repeated sphincter trauma, mucosectomy, handsewn anastomosis, decreased small bowel length in the patients who need to undergo redo procedures, and decreased compliance of a chronically inflamed pouch in patients who require a revisional SP.[55]

No direct correlation of functional results and QoL has been firmly established.[55] In MacLean and colleagues'[55] series, despite the poorer functional outcomes, the QoL of pouch reconstruction patients was similar to that for patients who had a successful initial IPAA. Satisfaction rates were reported at high levels throughout the few studies that incorporated this important variable in their SP patients' follow-up.[36,48,67,83,84,89,105] The latter results apparently originate from the patients' contentment with maintaining their pouch and their ability to continue their lives without a stoma.

Table 5. Quality of Life Outcomes and Patient Satisfaction

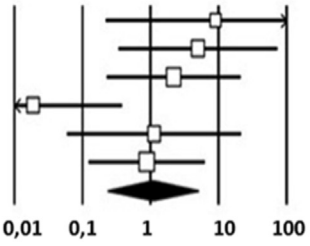
First author	Year	After salvage procedure, n	Evaluated, n	Quality of life outcomes and patient satisfaction
Ogunbiyi[36]	1997	30	16 with successful salvage	10 patients: good or excellent function; 6 patients: satisfied (although they had 9 BMs/day, 2–4 soiling episodes/week, necessitating pads)
Farouk[43]	1998	38	38	Of patients with pelvic sepsis: restricted work activity: 39%, domestic activities: 19%, travel: 47%, recreation: 47%, sexual activity: 29%; restrictions: not significantly different from patients without septic complications; 7 women who had pelvic sepsis: postoperative dyspareunia
Saltzberg[48]	1999	29	9 with successful redo procedure	All patients reported satisfaction with outcomes, 6 very satisfied, 2 moderately satisfied, 1 satisfied
MacLean[55]	2002	57	28	72% of patients usually or always felt well; 92% of patients usually or always had a good appetite; 60% of patients usually or always had a good energy level; 16% of patients believed that their bowel function interfered with daily activities; 84% of patients rated their physical health as good to excellent; 88% of patients believed their emotional and psychological health, confidence, and self-esteem were good to excellent; >80% of patients: unrestricted, or only mildly restricted, in participating in sports, hobbies, and leisure activities; 76% of patients: unrestricted or only mildly restricted in pursuing their career or educational objectives
Shen[63]	2004	19	19	CGQL scores after endoscopic stricture dilation: 0.69 ± 0.08 (week 8), 0.71 ± 0.11 (week 16) (significantly better than baseline CGQL scores: 0.69 ± 0.08, $p < 0.007$)
Loriau[68]	2005	1	1	Normal social, work, and sexual activities
Dehni[67]	2005	64	18 (transanal) 40 (abdominoperineal)	Degree of satisfaction: good to excellent in 13 transanal and 27 abdominoperineal patients; acceptable to poor: 5 transanal and 13 abdominoperineal patients
Remzi[83]	2009	241	126	Social restrictions: 19%, work restrictions: 24%, sexual restrictions: 23%; quality of life: 7.47 ± 2.36; energy level: 6.78 ± 2.58; happiness with results of surgery: 8.12 ± 2.2; CGQL score: 0.73 ± 0.22; pouch surgery again? 99% of patients; recommend pouch surgery: 98% of patients
Ortega-Deballon[84]	2009	3	3	GIFO score: 8.3 (mean 0–10); SF-36 improved after surgery; pouch surgery again?: All 3 patients; recommend pouch surgery: all 3 of patients; all 3 patients: feeling in good health (score, 3; scale, 1–5), active and optimistic about life and the future
Kirat[89]	2011	71	53	Social restrictions: 22.6%; work restrictions: 26.4%; sexual restrictions: 22.6%; quality of life: 7.7 ± 1.7; quality of health: 7.4 ± 1.7; quality of energy: 6.7 ± 1.2, CGQL score: 0.7 ± 0.1; happiness with surgery:8 ± 2.1; pouch surgery again?: 84.9% of patients; recommend pouch surgery: 90.5% of patients
Mennigen[92]	2012	12	8	SIBDQ score: 5 ± 0.5 (optimum: 7); GIQLI score: 95.8 ± 8.4 (optimum: 144)

BM, bowel movement; CGQL, Cleveland Global Quality of Life; GIFO, Gastro-Intestinal Functional Outcome; GIQLI, Gastrointestinal Quality of Life Index; SIBDQ, Short Inflammatory Bowel Disease Questionnaire.

Reference	No of patients	Odds ratio	Lower limit	Upper limit	Z-value	p-value
[27]. Poggioli et al, 1993	2 vs 4	9,000	0,223	362,480	1,165	0,244
[36]. Ogunbiyi et al, 1997	6 vs 8	5,000	0,344	72,767	1,178	0,239
[47]. Fonkalsrud et al, 1999	7 vs 99	2,190	0,230	20,828	0,682	0,495
[48]. Saltzberg et al, 1999	9 vs 9	0,019	0,001	0,377	-2,596	0,009
[72]. Johnson et al, 2005	2 vs 10	1,125	0,060	21,087	0,079	0,937
[79]. Shawki et al, 2009	7 vs 16	0,880	0,125	6,192	-0,128	0,898
Total	33 vs 146	1,080	0,233	0,098	0,098	0,922

Statistics for each study

Odds ratio and 85% CI

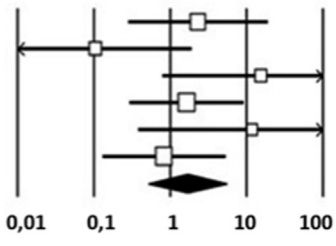


Favors "redo" Favors "revisional"

Reference	No of patients	Odds ratio	Lower limit	Upper limit	Z-value	p-value
[36]. Ogunbiyi et al, 1997	10 vs 6	2,333	0,287	18,965	0,793	0,428
[47]. Fonkalsrud et al, 1999	58 vs 7	0,105	0,006	1,907	-1,523	0,128
[48]. Saltzberg et al, 1999	11 vs 9	15,696	0,805	306,185	1,817	0,069
[60]. Shah et al, 2003	44 vs 6	1,647	0,298	9,107	0,572	0,567
[72]. Johnson et al, 2005	10 vs 2	12,000	0,384	374,837	1,415	0,157
[79]. Shawki et al, 2009	21 vs 7	0,833	0,131	5,297	-0,193	0,847
Total	154 vs 37	1,699	0,524	5,512	0,883	0,377

Statistics for each study

Odds ratio and 85% CI

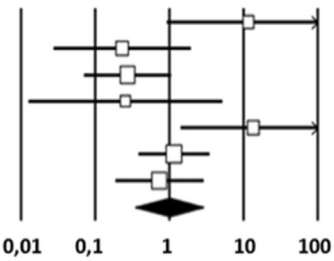


Favors "local/perineal" Favors "redo"

Reference	No of patients	Odds ratio	Lower limit	Upper limit	Z-value	p-value
[36]. Ogunbiyi et al, 1997	10 vs 8	11,667	0,922	147,563	1,898	0,058
[47]. Fonkalsrud et al, 1999	58 vs 99	0,231	0,028	1,923	-1,356	0,175
[48]. Saltzberg et al, 1999	11 vs 9	0,273	0,071	1,043	-1,898	0,058
[58]. Gorfine et al, 2003	47 vs 4	0,256	0,013	5,156	-0,889	0,347
[72]. Johnson et al, 2005	10 vs 10	13,500	1,421	128,258	2,266	0,023
[76]. Raval et al, 2007	59 vs 25	1,159	0,387	3,468	0,264	0,792
[79]. Shawki et al, 2009	21 vs 16	0,733	0,188	2,857	-0,447	0,655
Total	216 vs 37	1,002	0,347	2,896	0,004	0,997

Statistics for each study

Odds ratio and 85% CI



Favors "local/perineal" Favors "revisional"

Figure 2. Forest plots and results of meta-analyses comparing healing rates of redo vs revisional, redo vs local/perineal, and revisional vs local/perineal salvage procedures. Squares indicate point estimates of treatment effect (odds ratio [OR]), with the size of the square representing the weight attributed to each study and 95% CI indicated by horizontal bars. The diamond represents the summary ORs from the pooled studies with 95% CI. The differences between the first and the second group of the pairs under comparison are not significant.

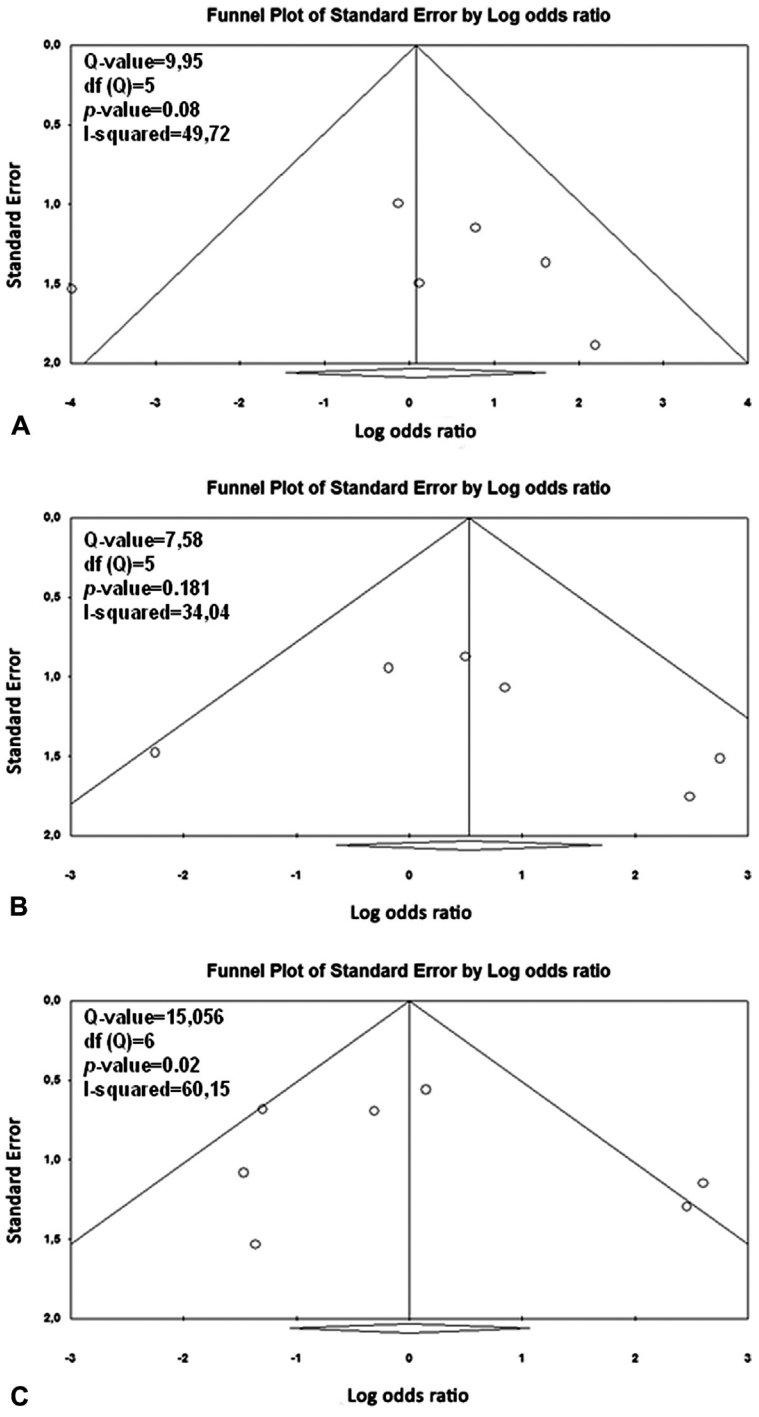


Figure 3. Funnel plots and heterogeneity analysis of studies comparing (A) redo vs revisional, (B) redo vs local/perineal, and (C) revisional vs local/perineal salvage procedures. Cochran's Q test was calculated as the weighted sum of squared differences between individual studies' effects. Q statistics follow chi-square distribution with $k - 1$ degree of freedom (df), where k is the number of the studies. Low p value (<0.1) means significantly heterogeneous results. $Q > k - 1$ suggests statistical heterogeneity. I^2 index describes the percentage of variance across studies that is due to significant heterogeneity rather than random chance. Subfigure A and C demonstrate substantial heterogeneity (I^2 index $>50\%$), while subfigure B demonstrates moderate heterogeneity (30% to 50%).

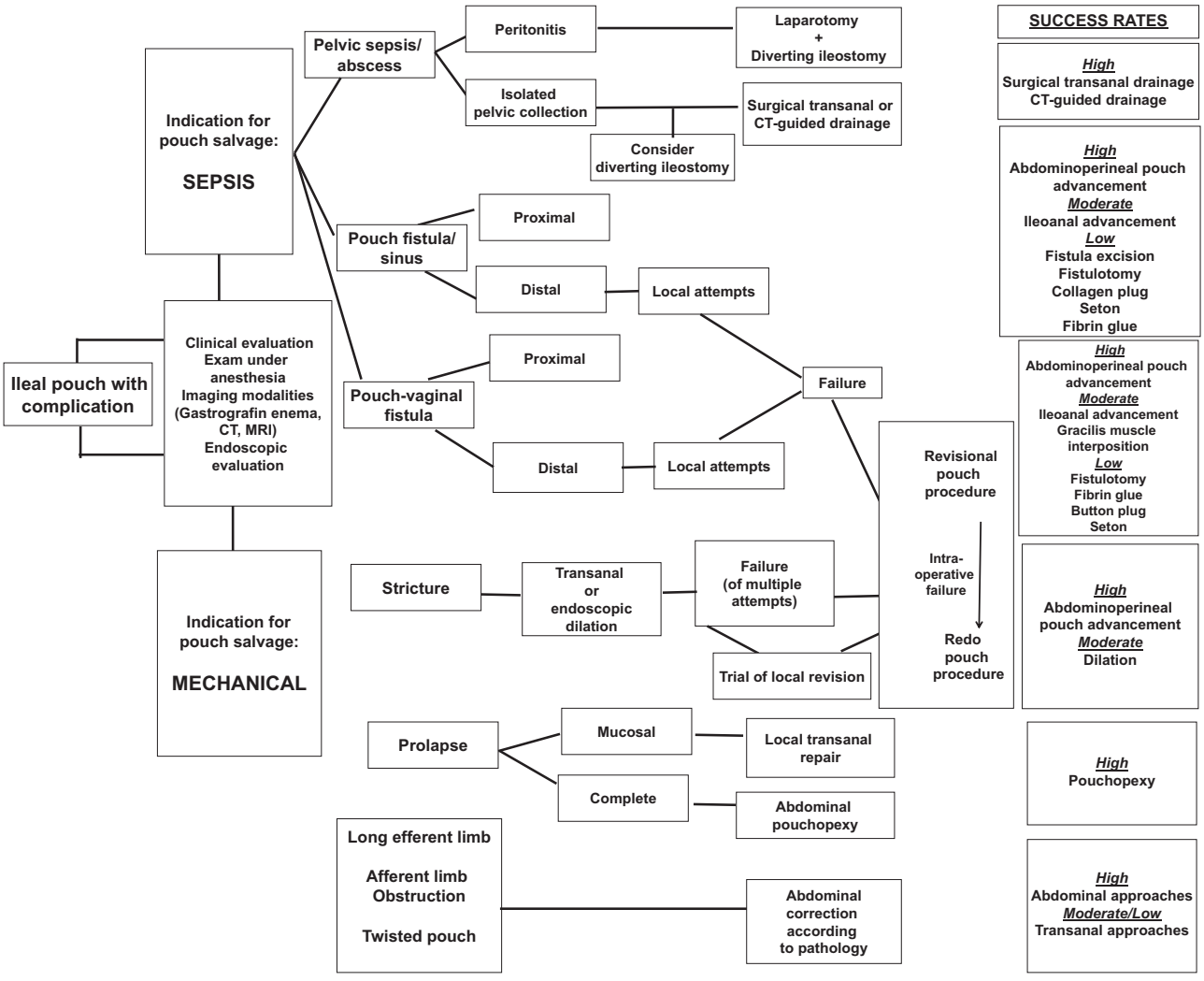


Figure 4. Proposed algorithm for managing pouch complications and relative success rates of the various salvage options.

CONCLUSIONS

The general trends observed in the studies under review agree with the application of revisional SPs maintaining the old pouch and, if this is not feasible, to substitute it with a new one; this usually follows a number of attempts for locally controlling the pelvic sepsis or, if possible and if the conditions permit, to locally correct the pathologies. The relative change in indications due to reduced use of certain pouch configurations in common practice has led to better understanding of the optimal sequential use of the techniques available in the current therapeutic options. The introduction of minimally traumatic, endoscopic or imaging-guided techniques will be followed by a paradigm shift in the types of procedures that will eventually remain widely accepted and be commonly practiced. Emerging novel techniques have yet to be validated by larger studies with longer follow-up. Accumulating results with periodically updated experiences from specialized institutions will help clarify the role of SP and guide future therapy.

Author Contributions

Study conception and design: Theodoropoulos, Choman, Wexner

Analysis and interpretation of data: Theodoropoulos, Choman, Wexner

Drafting of manuscript: Theodoropoulos, Choman, Wexner

Critical revisions: Theodoropoulos, Choman, Wexner

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APPENDIX 1.

Indications for salvage procedures

The indications (number of patients in parentheses) for SPs were as follows:

Septic: pelvic sepsis/abscess (redo SPs, n = 6; revisional SPs, n = 38; local/perineal SPs, n = 136); anastomotic leak/separation (redo SPs, n = 2; revisional SPs, n = 10; local/perineal SPs, n = 6); PVF (redo SPs, n = 13; revisional SPs, n = 64; local/perineal SPs, n = 174); peri-pouch fistula/sinus other than PVF (redo SPs, n = 4; revisional SPs, n = 34; local/perineal SPs, n = 81).

Mechanical: IPAA stenosis (redo SPs, n = 4; revisional SPs, n = 108; local/perineal SPs, n = 151); poor emptying (redo SPs, n = 11); long efferent limb (redo SPs, n = 5; revisional SPs, n = 31; local/perineal SPs, n = 61); retained rectum (redo SPs, n = 3; revisional SPs, n = 31); ischemic pouch (redo SPs, n = 1; revisional SPs, n = 4); pouch prolapse (redo SPs, n = 2; revisional SPs, n = 42; local/perineal SPs, n = 31); straight IPAA (redo SPs, n = 1; revisional SPs, n = 17); small-volume reservoir (redo SPs, n = 13); afferent limb obstruction (redo SPs, n = 28); pouch septum (redo SPs, n = 5; revisional SPs, n = 16); twisted pouch (redo SPs, n = 5); sphincter dysfunction/incontinence (redo SPs, n = 5; revisional SPs, n = 8).

Inflammatory: (redo SPs, n = 3; revisional SPs, n = 2).

Neoplastic changes: (redo SPs, n = 1; revisional SPs, n = 2).